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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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SUGHRUE, MION, ZINN, MACPEAK & SEAS, PLL
2100 PENNSYLVANIA AVENUE, N.W.
WASHINGTON DC 20037-3213

EXAMINER	
MORAN, M	
ART UNIT	**PAPER NUMBER**
1631	9

DATE MAILED: 10/25/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/691,053	AGUR ET AL.	
	Examiner	Art Unit	
	Morjorie Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-300* is/are pending in the application.

4a) Of the above claim(s) *66-233 and 332-465* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-65,234-331 and 466-509* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

In view of the amendments to the claims filed 8/8/01, the objection to claim 5 and the rejection of claim 246 under 35 USC 112 are hereby withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

The information disclosure statement filed 8/21/01 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 as set forth below. It has been placed in the application file, but all of the information referred to therein has not been considered as to the merits. Those references which have been considered are indicated by the examiner's initials. Those references which have NOT been considered are crossed out. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1). The reference by Hassin Agur disclosed on page 2 of the IDS has not been considered as there is not indication of the source of the article (i.e. name, volume number, etc.), not its date of publication. The reference by Athanassios et al. disclosed on page 4 of the specification has not been considered as the article itself is not among those included with the IDS. It is noted that a paper was filed which compares "Optimata's claims" and the state of the art, wherein the teachings of various references is summarized and compared to "work" by the assignee of the instant invention (Optimata). Athanassios' paper is among those summarized in the "comparison" paper, but the entirety of the article by Athanassios is not present. It is further noted that the "comparison" paper submitted has no indication of author, origin, or place or date of publication, and therefore is not a reference which can be properly

recited and considered in an IDS. Several articles/references were received which are not included on the IDS. Applicant is reminded that in order for a reference to be fully considered and made of record, it must be properly recited on an IDS which is properly filed with the USPTO, along with any required fees, petitions, etc.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

In response to applicant's argument that "there is no specific requirement in the law or in rules of practice as to the explicit wording" for identifying citizenship, and to applicant's request that the examiner point to the statute that requires that a country (e.g. Israel) be explicitly stated as opposed to a citizenship (e.g. Israeli), applicant's attention is drawn to 37 CFR 1.63 (a) (3) which explicitly states that an oath or declaration must: "Identify the country of citizenship of each inventor".

The rule does not state that the citizenship of each inventor must be identified, but states unambiguously that a COUNTRY must be identified. While it is clear from the currently filed declaration that the inventors are Israeli citizens, the declaration does not conform to 37 CFR 1.67 (a) as previously set forth and maintained above, therefore a new declaration identifying a country of citizenship must be filed.

Claim Objections

Claims 5, 8, 30, 54, 63, 278, 300, 320, 329, 241, 255, 269, 276-278, 296, 298-300, 473, 487, 501 are objected to because of the following informalities: the term "including" in line 2 of

each of claims 5, 30, 54, 63, 278, 300, 320, and 329 should be --includes--. In addition, the examiner recommends using terms known to be "open" or "closed" claim language such as --comprises-- in place of terms such as "includes". The term "Thrompocyte" in claims 30, 278, and 300 should be --Thrombocyte-- or --thrombocyte--. See below regarding capitalization. Claim 8 recites the abbreviations "PK" and "PD". These are abbreviations commonly used in the art and the full terms are recited elsewhere in the claims, therefore they are not indefinite. For clarity, the examiner recommends that the full terms be recited with their associated abbreviations the first time the abbreviations are recited in the claims; e.g. --pharmacokinetic (PK)--. In claims 241, 255, 269, 473, 487, and 501, the term "group" should be --groups--, twice, in line 2 of each claim. In claims 276 and 298, the term "mathematical" in line 2 should be --mathematically--. In claims 276 and 298, lines 2 and 3 of each, and in claims 277 and 299, line 1 of each, the term "populationss" should be --populations--. In claim 296, the term "Method" in line 1 should be --method--. Appropriate correction is required.

The term "incorporates" in claims 236, 250, 264, 285, 468, 482, and 496 is interpreted to have the same meaning as --comprises--. As "incorporates" may also be interpreted to be a verb, the examiner recommends that the term "incorporates" be replaced with --comprises-- for clarity.

Claim Rejections - 35 USC § 112

Examiner's note: The terms "contains", "containing", "include", "including", and any other bridging term which is not specifically defined in the specification recited in the claims is interpreted by the examiner to be open claim language, equivalent to "comprises" or "comprising".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-65, 234-331 and 466-509 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 50 recite a system comprising a system model modifier, "wherein said system model is modified..." Similarly, claims 234 and 248 recite a system comprising a system model modifier, "wherein said cancer system model is modified..." and claim 506 recites a computer program product comprising a system model modifier code, "wherein said system model is modified...". The claims are directed to products (systems and computer program), not methods, but each claim appears to recite a method step (i.e. of modifying a model). It is unclear what limitation of the system or code applicant intends in each claim, therefore the claims are indefinite.

Claims 2, 27, 51, 60, 235, 249, 263, 275, 297, 317, 326, 467, 481, 495, 507 and 509 each recites the term "realistic" with regard to a model. The term is recited many times in the specification but is not defined anywhere. The term "realistic" as applied to a model may have many meanings in the art; e.g. three-dimensional; approximating "real-time" interactions (e.g. during digestion); approximating actual or "realistic" physiological conditions (e.g. of pH, temperature, salt, etc.); etc. As one skilled in the art would not know what limitation of the model is intended by the term "realistic", the claims are indefinite.

Claims 5, 30, 54, 63, 278, 300, 320, and 320 recite the phrase "cell population with at least one disease is one of cancer cells, ..." It is unclear whether applicant intends to limit his "cell population with at least one disease" to cancer cells, or intends to limit the diseased cell population to one type of cancer cell, or intends to limit the diseased cell population to a single cancer cell, or intends some other limitation, therefore the claims are indefinite. It is noted that

the claims recite "..one of cancer cells, and diseased bone marrow cells..." If applicant actually intends to limit the diseased cell population to cancer cells or diseased bone marrow cells, then this rejection may be overcome by deleting the comma after "cancer cells" in line 2 of each claim.

Claims 5, 30, 54, 63, 278, 300, 320, and 320 recite diseased bone marrow cells "including diseased Neutrophil cells and diseased Thrombocyte cells." A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, the claims recite the broad recitation diseased bone marrow cells, and the claim also recites diseased Neutrophil cells and diseased Thrombocyte cells, which is the narrower statement of the range/limitation.

Claims 5, 30, 54, 63, 278, 300, 320, and 320 recite the capitalized terms "Neutrophil" and "Thrombocyte". The terms "neutrophil" and "thrombocyte" are not proper nouns, but usually refer to "generic" cell types (i.e. not a particular line or clone) and are therefore not usually capitalized. Due to the use of capitalized terms, it is unclear if applicant actually intends any neutrophilic or thrombocytic cells, or intends a specific cell line or clone (e.g. a neutrophil cell

line to model a specific disease which is deposited in accordance with USPTO deposit regulations), therefore the claims are indefinite.

Claims 7, 32, 56, 65, 280, 302, 322, and 331 are generally confusing and are therefore indefinite. Each claim recites that a treatment specific process "is interactions involving one of a group comprising...". The entire phrase is confusing, therefore the claims are indefinite.. If applicant intends that the treatment specific process comprise various interactions, then the examiner recommends that the term "is" be replaced with --comprises-- before "interactions" in line 1 of each claim. In addition, it is unclear what is meant by an "interaction involving" the members of the recited group. For example, what is meant by an interaction involving (a) pharmacokinetic?

Line 2 of each of claims 7, 32, 56, 65, 280, 302, 322, and 331 recites "pharmacokinetic, pharmacodynamic, cytostatic, cytotoxic" but do not recite if these are methods, models, interactions, reactions, etc., therefore the claims are further indefinite.

Claims 7, 32, 56, 65, 280, 302, 322, and 331 each recites "with associated biological processes" in lines 3-4. It is unclear what prior phrase or limitation recited in each claim is intended to be "with" associated biological processes. In addition, it is unclear what the biological processes are intended to be associated with, therefore the claims are also indefinite.

Claims 8, 57, 281, and 323 each recite "the biological process" in line 2. There is no antecedent basis for this phrase in the claims, therefore the claims are indefinite. This rejection may be overcome by replacing "the" with --a-- in each claim.

Claims 10 and 33 recite a selector which "incorporates" parameters "in performing selection". This appears to be a method step. The claims are drawn to systems, not methods, therefore it is unclear what limitation of the systems are intended by the recitation that a selector "incorporate" parameters while "performing" a selection. If applicant intends that the selector

comprise parameters wherein said parameters may be accessed by the selector, then the examiner recommends rewriting the claims to clearly recite the limitation of the claimed products (systems) which applicant intends.

Claims 11 and 34 recite the phrase "wherein said incorporation is done by using...". Again, this appears to be a method step. The claims are drawn to products, not methods, therefore it is unclear what limitations of the claimed systems is intended by the phrase. In addition, it is unclear what step or limitation is intended by the term "using", as the term is not defined in the specification and may have many meanings in the art. For these reasons, the claims are indefinite.

Claims 12, 35, and 305 recite a broad limitation followed by a narrower limitation, therefore the claims are indefinite. See above regarding broad and narrow limitations in the same claim. The broad limitation recited in each claim is "disease stage"; the narrower limitation is "cure".

Claims 12. 35, and 305 recite a phrase in parentheses. Use of parentheses in these claims renders the claims indefinite as it is unclear whether applicant intends the phrase in the parentheses to be a positive limitation of the claims.

Claims 12, 35, and 305 recites the phrase "selected from a group comprising...". It is unclear if applicant intends --selected from a group consisting of...--, or intends --comprising--, therefore the claims are indefinite.

Claims 13 and 36 recite the phrase "wherein a user can input" coefficients "to adjust" a fitness function. This appears to be a method step. The claims are directed to a product (system), therefore it is unclear what limitation of the claimed products is intended by the recited phrases, and the claims are indefinite.

Claims 17-18, 40-41, 290-291, and 310-311 recite that selection of treatment protocols "incorporate" cytotoxic effects or drug efficacy. It is unclear what applicant intends by a selection which "incorporates" cytotoxic effects or drug efficacy, therefore the claims are indefinite.

Claims 19 and 42 recite a selector which "performs" a selection. This appears to be a method step. This appears to be a method step. The claims are directed to a product (system), therefore it is unclear what limitation of the claimed products is intended by the recited phrases, and the claims are indefinite.

Claims 20, 43, 293, and 313 recite heuristics "being used to perform searching and selecting". This appears to be a method step. Claims 20 and 43 are directed to a product (system), therefore it is unclear what limitation of the claimed products is intended by the recited phrases, and the claims are indefinite. Claims 293 and 313 are directed to methods and are not indefinite for the above reason. However, it is unclear what step is intended by the phrase "being used", and it is unclear what limitation of the heuristics is intended by the recited phrase, therefore all of claims 20, 43, 293 and 313 are indefinite.

Claims 22, 45, 295 and 315 recite broad and narrow limitations and are therefore indefinite. See above regarding broader and narrower limitations in the same claim. The broader limitation in each claim is "treatment strategy", the narrower limitation is "types of treatment". If applicant intends a different limitation by the recitation of "including types of treatment", then it is unclear what that limitation is, and the claims are still indefinite.

Regarding claims 22, 45, 295, and 315, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 23 and 46 recite a system which "is implemented" over a computing system. This appears to be a method step. Claims 23 and 46 are directed to a product (system), therefore it is unclear what limitation of the claimed products is intended by the recited phrases, and the claims are indefinite.

Claims 25 and 48 recite the phrase "a user uses the system". This appears to be a method step. The claims are directed to a product (system), therefore it is unclear what limitation of the claimed products is intended by the recited phrases, and the claims are indefinite. Applicant is advised that an a method of use of a product is not a limitation of that product.

Claim 50 recites a narrower limitation and a broader limitation, therefore the claim is indefinite. See above regarding narrower and broader limitations in the same claim. The broader limitation is "plurality of protocols", the narrower limitation is "no treatment".

Claims 50 and 59 recite that a biological process "could be" related to healthy or diseased processes. Conditional language renders a claim indefinite as it is unclear whether the limitations following the conditional language are intended to be claim limitations. This rejection may be overcome be replacing "could be" with --is-- in each claim.

Claims 234, 248, 262, 466, 481, and 494 each recites a narrower limitation and a broader limitation. See above regarding narrower limitations and broader limitations in the same claim. The broader limitation is "treating cancer using drugs", the narrower limitation is "chemotherapy".

Claims 237, 251 and 265 recite cells "entering a compartment always enter a first sub-compartment". This appears to be a method step. The claims are directed to products (systems), therefore it is unclear what limitation of the claimed systems is intended, and the claims are indefinite.

Claims 238, 252, and 266 recite that a model "traces development" of cancer cells "using" a set of parameters by "calculating" a number of cells "using" stepwise equations. These appear to be a number of method steps. Applicant should note that a method of use (e.g. of the model) is not a limitation of a product. It is unclear what limitation of the claimed products (systems/models) is intended, therefore the claims are indefinite.

Claims 239, 253, and 267 recite that a probability vector "is used". This appears to be a method step. The claims are directed to products (systems), therefore it is unclear what limitation of the claimed systems is intended, and the claims are indefinite.

Claims 240, 254, and 268 recite that set control functions "determine" an outcome. This appears to be equivalent to a measuring step, and therefore appears to be a method step. The claims are directed to products (systems), therefore it is unclear what limitation of the claimed systems is intended, and the claims are indefinite.

Claims 240, 254, 268, 472, 486, and 500 recite that control functions "depend on" various factors. It is unclear what limitation of the control functions is intended by the recitation of "depend on"; i.e. do the control functions comprise the recited factors, are the control functions adjusted for or by the recited factors, etc., therefore the claims are indefinite.

Claims 241, 255, and 269 recite that a tumor "is modelled". This appears to be a method step. The claims are directed to products (systems), therefore it is unclear what limitation of the claimed systems is intended, and the claims are indefinite. If applicant intends that a tumor model comprise the recited combination of cells, then this rejection may be overcome by replacing "tumor is modeled as" with --tumor model comprises-- in line 1 of each claim.

Claims 242, 256, and 270 each recites "in each step" in line 1. The claims are directed to systems (products) and do not recite steps. As the entirety of each claim is directed to step

limitations, it is unclear what limitation of the claimed systems is intended and the claims are indefinite.

Claims 244, 258, and 272 recite that various effects "are incorporated" into the model. This appears to be a method step. The claims are directed to products (systems), therefore it is unclear what limitation of the claimed systems is intended, and the claims are indefinite. If applicant intends that the model comprise the recited effects, then the claims should be rewritten to clearly reflect the limitations of the model intended by applicant.

Claims 244, 258, 272, 476, 490, and 504 recite the terms "PK" and "PD". These are commonly used abbreviations in the art; however, it is unclear what limitation of a model is intended by "incorporation" of PK or PD into the model (i.e. models to not usually comprise PD or PK per se; does applicant actually intend that the model comprise a PK effect or PD effect?), therefore the claims are indefinite.

Claims 245, 259, and 273 recite that a toxicity "is incorporated" into the model. This appears to be a method step. The claims are directed to products (systems), therefore it is unclear what limitation of the claimed systems is intended, and the claims are indefinite. If applicant intends that the model comprise the recited toxicity (data, levels, information?), then the claims should be rewritten to clearly reflect the limitations of the model intended by applicant.

Claims 274, 296, and 466 recite methods of recommending an optimal treatment protocol, then recites steps culminating in selection of an optimal treatment. The claims do not recite any step of recommending a treatment, therefore it is unclear if the claims are directed to methods of selection or recommendation, and are indefinite. This rejection may be overcome by replacing "recommending" with --selecting-- in the preamble of each claim, if such an amendment is consistent with applicant's intent. Applicant is reminded that additional method

steps (e.g. added in amendment) must be fully supported an enabled by the originally filed specification.

Claim 291 recites that treatment protocols incorporate drug. The intended limitation is unclear, therefore the claim is indefinite. If this is due to a typographical error, then this rejection may be overcome by inserting --efficacy-- after "drug".

Claims 316, 325, 480, 494 recite methods of predicting progression of a biological process or cancer in the preamble, then recite steps of creating a model and selecting an optimal treatment protocol. As no predictive steps are recited in any of the claims, it is unclear whether the claims are intended to be directed to methods of prediction, or are intended to be directed to methods of selection. In addition, the claims do not recite any limitations with regard to *progression* of a process (e.g. disease) or cancer, or with regard to modeling *progression* of a biological process or cancer, therefore it is unclear if applicant actually intends methods as recited in the preamble of each claim. For these reasons, the claims are indefinite. Applicant is reminded that additional method steps (i.e. added in amendment) must be fully supported an enabled by the originally filed specification.

Claim 325 limits a biological process to be related to "healthy or diseased". It is unclear what is intended to be "healthy or diseased"; e.g. organism, cell, tissue, etc., therefore the claim is indefinite.

Applicant is STRONGLY encouraged to fully review the claims for typographical and grammatical errors in addition to those set forth in the rejections and objections above.

Claim Rejections - 35 USC § 102

Claims 1, 18, 23-26, 41, 46-49, 274, 296, 506 and 508 are again rejected, as previously set forth in the office action of 5/8/01 under 35 U.S.C. 102(e) as being anticipated by BARRY *et al.* (US 6,081,786).

Applicant's arguments filed 10/10/01 have been fully considered but they are not persuasive. In response to the argument that BARRY does not teach a model, applicant's attention is drawn to col. 5, lines 8-13 wherein BARRY teaches that his computer system contains "a knowledge base of expert rules for determining available treatment options" and col. 7, lines 45-52 wherein BARRY teaches that his "expert system", also known as artificial intelligence, is a computer program which can *simulate* the judgment and behavior of a human, and teaches that the expert system contains a knowledge base and a set of rules for applying the knowledge base to each particular situation. Any method of simulation is a model, therefore BARRY's expert rules, when applied to his knowledge base (i.e. thereby simulating human judgment/choice), is interpreted by the examiner to be a model. BARRY's system is clearly computer-implemented, therefore applicant's arguments regarding a computer model are not persuasive. BARRY also teaches that his system may comprise mathematical formulae (col. 15, lines 50-55), and teaches that the system (rules) may be modified such that an output is changed (i.e. different recommendation for an optimal treatment) upon entry of patient information (col. 15, line 38-col. 16, line 25), therefore arguments with respect to a mathematical model and modification based on patient information are not persuasive.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a "bio-clinical scenario", a mathematical or computer model (the system is not limited to be a computer, therefore the "system model" is not limited to be a computer model), modification of the model

based on patient information (i.e. a method step) , and "modifying an overall bio-clinical scenario by manipulation of inherent biological factors) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). A step of modifying a model based on patient information is recited in claim 274 (directed to a method); however, BARRY teaches that his system and rules (model) can be modified based on patient information, as set forth above. None of the claims recite modification of a bio-clinical scenario nor manipulation of "inherent" biological factors.

For the reasons set forth, the examiner maintains that BARRY anticipates the claims.

Claim Rejections - 35 USC § 103

Claims 1-3, 6-19, 22-28, 31-42, 45-52, 55-61, 64-65, 234-235, 246-249, 260-263, 274-276, 279-292, 295-298, 301-312, 315-318, 321-327, 330-331, 466-467, 478-481, 492-495, and 506-509 are rejected under 35 U.S.C. 103(a) as being unpatentable over BARRY et al. (US 6,081,786) in view of FINK et al. (US 5,808,918).

Applicant's arguments filed 10/10/01 have been fully considered but they are not persuasive. In response to applicant's argument that FINK does not teach a "realistic" biological model, applicant's attention is drawn to col. 3, lines 12-23 wherein FINK teaches that her model "integrates all of the biological relationships that are known to exist" and are relevant to a particular disease, in order to provide a "dynamic executable model" for identifying new drug targets, better understanding key biological mechanisms, and assessing clinical information. FINK also teaches that her model may be developed to include "the biology to a level of detail necessary to link variations in clinical outcomes to the variation in a patient's basic biology" (col. 6, lines 64-67). A dynamic model which integrates all of the known biological relationships with

regard to a particular disease, and wherein variations of clinical outcomes (a real-life result) can be linked to variations in a patient's basic biology (real-life data) is a "realistic" a model for that disease, therefore the examiner maintains that FINK teaches a "realistic" biological model. It is noted that FINK also teaches that if "the model does not duplicate real life outcomes in the area of interest, then it is not valid and requires modification" (col. 7, lines 58-60), thus clearly teaching that FINK considers her model to be one which duplicates real life outcomes; i.e. is "realistic". Applicant's arguments that FINK's model is "simplistic" and does not include "constitutive equations encapsulating a biological mechanism" are not persuasive as the claims do not recite constitutive equations nor any degree of "complexity" (as opposed to FINK's argued "simplicity"). Applicant is reminded although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims (see above). Applicant further argues that FINK does not teach incorporation PK or PD data, or data regarding cytostatic or cytotoxic effects with regard to cells, into her model such that a clinical prediction may be made. In response, applicant's attention is drawn to col. 12, line 45-col. 13, line 13 wherein FINK teaches incorporation of data regarding reduction of bacterial load by an antimicrobial agent (i.e. cytotoxic cell effects) into her model, and teaches incorporation of pharmacological effects, PK data, and dose implications in order to "identify biologic factors that have the greatest leverage on clinical outcomes in the particular disease." The examiner maintains that this is a teaching of incorporating the factors taught by FINK into her model in order to determine an optimal treatment for a particular disease. FINK's "dose implications" suggest drug interactions and side effects, and FINK specifically teaches incorporation of pharmacological properties into her model, therefore the arguments regarding drug "mechanisms", etc. set forth on page 10 of the response are not persuasive. FINK teaches that such "real life" effects as pain should be included in her model (col. 7, lines 55-60), teaches

inclusion of impact on biological factors, such as decrease of bacterial load (cytotoxicity, col. 12, lines 46-57), teaches inclusion of disease level (tumor or pathogen load, col. 11, lines 44-45), and teaches that her model must be modified until it appears to exhibit reasonable (real life) behavior (col. 11, lines 5-45), therefore arguments with regard a fitness function and included parameters are not persuasive. Applicant is reminded that the rejections is made over a combination of references wherein BARRY also teaches entry of side effects (e.g. anemia) and viral load (col. 15, lines 40-65) into his program/model to better fit the program/model to a particular patient. In response to the argument that FINK's dynamic model can not be combined with BARRY's "canned" program is not persuasive as both BARRY and FINK teach use of their models to predict optimal treatment and the information (output) from FINK's program could be used in place of or in addition to BARRY's expert rules. BARRY teaches that any of his computer program steps can be implemented by computer program instructions (col. 4, lines 26-40) and teaches at least one "module" which includes a therapy user interface that facilitates evaluation of various therapeutic treatments (col. 3, lines 45-50). As FINK's model is one which evaluates therapeutic treatments, the examiner maintains that the "dynamic" biological model of FINK, or information obtained therefrom, could successfully have been combined with program of BARRY. In response to the argument that neither BARRY nor FINK teach predicting progression of a disease, applicant's attention is drawn to col. 3, lines 18-23 wherein FINK teaches that her model may be used to demonstrate (predict) the course of a particular disease progression. In response to argument that BARRY nor FINK teach systems or methods of recommending optimal treatment for cancer, applicant's attention is drawn to col. 6, lines 52-56 wherein BARRY teaches that treatment for a variety of cancers may be predicted using his system and method. In response to arguments that the prior art does not teach or suggest "the cancer system model disclosed in the specification", as argued on pages 13-14 of the response,

applicant is reminded although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims (see above). For all of the reasons set forth above, the examiner maintains the rejection.

Claims 1-65, 234-331 and 466-505 are rejected under 35 U.S.C. 103(a) as being unpatentable over BARRY et al. (US 6,081,786) in view of FINK et al. (US 5,808,918) as applied to claims 1-3, 6-19, 22-28, 31-42, 45-52, 55-61, 64-65, 234-235, 246-249, 260-263, 274-276, 279-292, 295-298, 301-312, 315-318, 321-327, 330-331, 466-467, 478-481, 492-495, and 506-509 above, and further in view of THALHAMMER-REYERO (US 5,930,154).

Applicant's arguments filed 10/10/01 have been fully considered but they are not persuasive. In response to the arguments (in summary) that THALHAMMER-REYERO does not teach a bio-clinical model, does not teach modifying a system with patient-specific information, does not teach a cancer model system or treatment of cancer, and does not teach selection of optimal treatments, applicant is reminded that the rejection is made over a combination of references wherein BARRY and FINK teach and/or make obvious all of the argued limitations. THALHAMMER-REYERO is not relied upon for a teaching of a biological model per se, but is relied upon for her teaching of modeling cells in an integrated computer-based system (abstract and col. 23), and her teaching that modeling cell states and transitions is of major importance in simulating the behavior of biological systems (col. 7, lines 30-40), which provides a motivation for combining THALHAMMER-REYERO with BARRY and FINK. In response to the argument that THALHAMMER-REYERO does not teach sub-compartments, applicant's attention is drawn to col. 23, lines 31-42 wherein THALHAMMER-REYERO teaches that G1 state cells may be further compartmentalized (i.e. into sub-compartments G1.1 and G1.2). THALHAMMER-REYERO further teaches that G1.1. cells are early G1 phase cells and G1.2 are late phase G1

cells, therefore cells necessarily enter a first sub-compartment (G1.1) upon entering the G1 compartment, thus applicant's arguments with regard to sub-compartments are not convincing. In response to the argument that a combination of BARRY, FINK , and THALHAMMER-REYERO would not have "worked" due to the different kinds of programs taught by each, the examiner maintains that the *information* taught by each reference may have successfully been combined as all teach computer systems and methods for predicting various biological functions. One skilled in the art would reasonably have expected success in including the cellular modeling information of THALHAMMER-REYERO in the method of FINK because FINK teaches that information regarding cell pools and regulators may be included in her model (e.g. col. 4, line 62-col. 5, line 8). The examiner maintains that information obtained from the model of FINK may be successfully incorporated into BARRY's system, as set forth above. Since the combination of FINK and THALHAMMER-REYERO would be expected to result in more accurate information, as taught by THALHAMMER-REYERO (above), the examiner maintains that information from a combination of FINK and THALHAMMER-REYERO may also be successfully combined with BARRY. It is noted that the claims are directed to systems and methods, and do not recite specific programs. For the reasons set forth above, the examiner maintains the rejection.

Election/Restrictions

Claims 66-233 and 332-465 are again withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention.

Conclusion

Claims 1-65, 234-331 and 466-509 are rejected; claims 5, 8, 30, 54, 63, 278, 300, 320, 329, 241, 255, 269, 276-278, 296, 298-300, 473, 487, 501 are objected to; claims 66-233 and 332-465 are withdrawn..

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3388.

Marjorie A. Moran
October 22, 2001

MICHAEL P. WOODWARD
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600